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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/071,299	02/07/2002	Qinghong Yang	10752-014-999	1129

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GRAY CARY WARE & FREIDENRICH LLP
153 TOWNSEND
SUITE 800
SAN FRANCISCO, CA 94107

EXAMINER

MORAN, MARJORIE A

ART UNIT	PAPER NUMBER
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1631

DATE MAILED: 09/30/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/071,299	YANG, QINGHONG	
	Examiner	Art Unit	
	Marjorie A. Moran	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 May 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-26 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-26 is/are rejected.
- 7) ☒ Claim(s) 1-3 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 07 February 2002 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____ |

Information Disclosure Statement

The IDS's filed 7/10/02 and 9/19/02 have been considered in full. Applicant is advised that a *Search Report* for a PCT is not considered a foreign *patent* document and therefore is not properly listed under the "Foreign Patent Documents" section of an IDS. Further, the "date of publication" for a Search report is generally considered to be its mailing date, not the date of filing of the related PCT. The examiner has altered the IDS filed 7/10/02 so that the Search Reports listed therein are properly listed under "Other Documents" and properly reflect the mailing date of each. The Search Reports are initialed to indicate that each has been considered.

While searching the prior art, the examiner found numerous US patents, US published applications US patent applications, and foreign patents which recite similar claims, overlapping inventors, identical titles and/or the same assignee as the instant application. As set forth in MPEP 2001.06(b), the individuals covered by 37 CFR 1.56 have a duty to bring to the attention of the examiner, or other Office official involved with the examination of a particular application, information within their knowledge as to other copending United States applications which are "material to patentability" of the application in question. As set forth by the court in *Armour & Co. v. Swift & Co.*, 466 F.2d 767, 779, 175 USPQ 70, 79 (7th Cir. 1972):

[W]e think that it is unfair to the busy examiner, no matter how diligent and well informed he may be, to assume that he retains details of every pending file in his mind when he is reviewing a particular application . . . [T]he applicant has the burden of presenting the examiner with a complete and accurate record to support the allowance of letters patent. See also MPEP § 2004, paragraph 9.

Accordingly, the individuals covered by 37 CFR 1.56 cannot assume that the examiner

of a particular application is necessarily aware of other applications which are "material to patentability" of the application in question, but must instead bring such other applications to the attention of the examiner. For example, if a particular inventor has different applications pending in which similar subject matter but patentably indistinct claims are present, that fact must be disclosed to the examiner of each of the involved applications. Similarly, the prior art references from one application must be made of record in another subsequent application if such prior art references are "material to patentability" of the subsequent application.

Specification

The abstract of the disclosure is objected to because it is not specifically directed to the subject matter of the instant claims. Appropriate correction is required. See MPEP § 608.01(b).

The disclosure is objected to because of the following informalities:

(1) the Brief Description of the Figures on page 4 of the specification does not include a description of the several views of the drawings (e.g. there is no "brief description" of FIGURES 1A and 1B). 37 CFR 1.74 requires that:

"When there are drawings, there shall be a brief description of the several views of the drawings and the detailed description of the invention shall refer to the different views by specifying the numbers of the figures and to the different parts by use of reference letters or numerals (preferably the latter)."

(2) the specification contains blank spaces correlated to attorney docket numbers; for example, on pages 3 and 15.

Appropriate correction is required. Applicant is reminded that any amendments to the specification must be fully supported by the originally filed disclosure in order to avoid introduction of new matter.

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. See page 28 of the specification, for example. Applicant is required to delete all embedded hyperlinks and/or other form of browser-executable code. See MPEP § 608.01.

Claim Objections

Claims 1 -3 are objected to because of the following informalities: the claims contain inappropriately placed periods. As set forth in MPEP 608.01(m): "Each claim begins with a capital letter and ends with a period. Periods may not be used elsewhere in the claims except for abbreviations. See *Fressola v. Manbeck*, 36 USPQ2d 1211 (D.D.C. 1995). " This objection may be overcome by replacing the periods after each letter (i.e. those indicating separate steps) with a parenthesis.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites the phrase "binding of tracer molecule" in step (c). It is unclear whether applicant intends --a-- tracer molecule (i.e. one different from that of the preceding claim steps) or intends --the-- tracer molecule (of the preceding claim steps), therefore the claim is indefinite.

The indefiniteness appears to be due to a typographical error, and may be overcome by inserting the appropriate article before "tracer" in step (c).

Claim 2 recites a step (c) of comparing binding of "said tracer molecule said detection molecule in b." This is nonsensical and grammatically incorrect. It is unclear if applicant intends comparison of binding of the tracer molecule --to-- the detection molecule with binding of the tracer molecule to another molecule, intends comparison of binding of the tracer molecule to the four-way complex of step (b) --with-- binding of the detection molecule to the four-way complex of step (b), or intends some other limitation, therefore claim 2 is indefinite.

Claim 2 recites the term "said test solution" and the phrase "without said four-way complex" in step (c). There is no antecedent basis for this term in the claim, therefore the claim is indefinite. Further, it is unclear what is intended to occur or be comprised in "said test solution"; i.e. is the entirety of step (c) to be carried out in a test solution or only binding of the tracer molecule to the detection molecule? If not, then what is comprised in the test solution? Further, it is unclear what is intended to be "without the four-way complex"; i.e. the test solution, or is one or more binding steps intended to occur "without" or in the absence of the four-way complex? As it is unclear what limitations are intended by the term and phrase listed above, both singly and together, claim 2 is indefinite.

Claim 2 recites "wherein reduced binding in b." in the penultimate line of step (c). No binding is recited in step (b), therefore it is unclear what "binding" is intended to be reduced. Further, step (c) recites a comparison step, not step (b), therefore it is unclear what is intended to be compared in step (b) in order to determine a "reduced" binding. For these reasons, claim 2 is indefinite.

The method steps intended for claim 2 are so unclear as to be unsearchable. Therefore, for purposes of applying the prior art, the examiner interprets claim 2 to be reciting the same or similar method steps as claim 1.

Claims 21 and 26 recite the term "cy dyes". The term is not one commonly used in the art and is not defined by the specification. As it is unclear what sort of dyes are intended to be "cy dyes", the claims are indefinite.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-26 are rejected under 35 U.S.C. 102(e) as being anticipated by YANG et al. (US 2002/0042061, filed 3/12/2001).

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the

inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

YANG teaches a method of detecting a difference in two nucleotide sequences by contacting the nucleotides with a detection molecule and a tracer molecule under conditions which allow the formation of a stable 4-way Holliday junction and which simultaneously allows for binding of the detection molecule to the Holliday junction and/or the tracer molecule, then determining that a difference in binding of the tracer molecule to the detection molecule in the presence and absence of the Holliday complex indicates a difference in the sequences of the nucleotides (paragraphs 80, 84-86, and 99), thereby anticipating claims 1-9 and 17-19. YANG teaches that his detection molecule may be a Ruv protein, or may be a Cce1, spCce1, or an Hjc protein (paragraph 89) and teaches that a tracer molecule may be labeled with a fluorophore (paragraph 99), specifically fluorescein, rhodamine, and other dyes (paragraph 93), thereby anticipating claims 10-26.

Claims 1-11 and 17-21 are rejected under 35 U.S.C. 102(b) as being anticipated by LISHANSKI et al. (IDS ref: US 6,013, 439).

LISHANSKI teaches a method of detecting differences between nucleic acid sequences wherein two nucleic acids are brought into contact under conditions which allow formation of a Holliday complex with branch migrations, wherein formation of a stable complex indicates that the nucleic acid strands are not identical, specifically, have a mutation (col. 16, line 23-col. 17, line 33). LISHANSKI teaches that his complex may be contacted with a receptor which binds to a feature of the complex, and a reporter molecule (col. 21, lines 22-30) and teaches that binding pairs may be used for detection of a complex wherein one member of the binding pair is labeled with a dye or fluorescent group (col. 15, lines 42). In this case, the

receptor or molecule complementary to the Holliday complex would be a "detection molecule" and the reporter or labeled member of a specific binding pair would be the "tracer molecule", therefore Examples 4 and 6 of LISHANSKI anticipate claims 1-9 and 17-21. . LISHANSKI specifically teaches that his reporter molecule may be labeled with fluorescein (col. 15, lines 38-42), and that his "detector molecule" can bind to a Holliday complex (col. 21, lines 27-30), thus claims 10-11 are anticipated.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over LISHANSKI et al. (IDS ref: US 6,013, 439) in view of MEZARD et al. (IDS ref: Nuc. Acids Res. (1999) vol. 27, no. 5, pp. 1275-1282).

Claims 1 and 2 recite a method of detecting a difference in the sequence of two nucleic acids molecules by contacting the molecules under conditions which allow a four-way complex

to form and allow branch migration, contacting the four-complex with a detection molecule and a tracer molecule, wherein the detection molecule binds to the four-way complex and the tracer molecule and determining that the nucleic acids sequences are different if tracer binding to the detection molecule is reduced in the presence of the four-way complex. Claim 3 limits the contacting of the nucleic acids with each other to be simultaneous with contact with the tracer and detector molecules. Claim 4 limits the methods to one wherein the four-way complex is resolved/completed if the nucleic acids are identical. Claim 5 limits the method to one wherein the four-way complex is not resolved/completed if the nucleic acids are not identical. Claim 6 limits the method to one wherein, if the nucleic acids are different, branch migration stops and the four-way complex is stabilized, but if the nucleic acids are identical, branch migration goes to completion. Claim 7 limits the difference in the nucleic acids to be a mutation, insertion, deletion, or single-base substitution. Claim 8 limits one of the nucleic acids to be DNA. Claim 9 limits the four-way complex to be a Holliday junction. Claim 10 limits the detection molecule to be one which selectively binds a Holliday junction. Claim 12 limits the detection molecule to be one from a specific list. Claim 13 limits the detection molecule to be thermostable. Claim 14 limits the tracer molecule to be a nucleic acid comprising a stable 4-way complex. Claim 15 limits the tracer molecule to be a nucleic acid comprising an immobile 4-way complex. Claim 17 limits the tracer molecule to be one which selectively binds the detection molecule. Claim 22 recites a tracer molecule comprising a label, and comprising a nucleic acid complex comprising a stable 4-way complex. Claims 16 and 23 limit the tracer molecule to comprise 1-4 oligonucleotides. Claims 18-19 and 24 limit the tracer molecule to comprise a detectable label, specifically one which generates a signal upon binding. Claims 20-21 and 25-26 limit the label to be a fluorescent one from a recited group.

LISHANSKI teaches method of detecting differences between nucleic acid sequences wherein two nucleic acids are brought into contact under conditions which allow formation of a Holliday complex with branch migrations, wherein formation of a stable complex indicates that the nucleic acid strands are not identical, specifically, have a mutation, as set forth above. LISHANSKI teaches that his complex may be contacted with a receptor; i.e. detection molecule which binds to a feature of the complex, and to a reporter molecule; i.e. tracer molecule, wherein the reporter molecule may be labeled with a dye or fluorescent group, also as set forth above. LISHANSKI specifically teaches that his reporter molecule may be labeled with fluorescein (col. 15, lines 38-42), and that his "detector molecule" can bind to a Holliday complex (col. 21, lines 27-30), as set forth above. LISHANSKI does not teach a detector molecule which one from the list recited in claim 12, does not specifically teach that his detector molecule is thermostable, nor does LISHANSKI teach a tracer/reporter molecule which is a nucleic acid molecule and comprises a 4-way complex and 1-4 oligonucleotides.

MEZARD teaches Ruv proteins which specifically bind to Holliday junctions to form complexes, wherein the complex formed is a stable 4-way complex comprising 4 oligonucleotides (p. 1275). MEZARD teaches that the complex can then bind to other Ruv proteins which are known to mediate branch migration (pp. 1275-1276).

It would have been obvious to one of ordinary skill in the art to have used a RuvB or other Ruv molecule taught by MEZARD as the detector molecule in the method of LISHANSKI where the motivation would have been to use any protein known to bind specifically to a Holliday (four-way) complex of nucleic acids, as suggested by LISHANSKI's teaching for use of receptors which bind to Holliday complexes. It would further have been obvious to have used the RuvA complex of MEZARD as the reporter/tracer molecule in the method LISHANSKI where the motivation would have been to use a stable molecule known to be capable of binding to the

Art Unit: 1631

detector molecule (i.e. RuvB), as suggested by the binding pairs of LISHANSKI, and where RuvB is known to also interact with a Holliday complex, as taught by MEZARD.

Conclusion

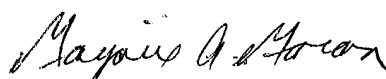
Claims 1-26 are rejected.

The prior art made of record and not relied upon which is considered pertinent to applicant's disclosure is LISHANSKI et al. (US 6,232,104).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marjorie A. Moran whose telephone number is (703) 305-2363. The examiner can normally be reached on Monday to Friday, 7:30 am to 4 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (703) 308-4028. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 305-3524.


MARJORIE MORAN
PATENT EXAMINER

mam